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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/574,461	11/30/95	BARONE	A 16528X-0155-

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HM12/1005

EXAMINER

PONNALURI, P

ART UNIT	PAPER NUMBER
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1627

DATE MAILED:

10/05/01

38

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trad marks

Office Action Summary

Application No.
08/574,461Applicant(s)
Barone et alExaminer
P. PonnaluriArt Unit
1627

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on Jul 19, 2001
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-8, 10-15, and 37-39 is/are pending in the application.
- 4a) Of the above, claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-8, 10-15, and 37-39 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

- 13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).
- a) ☐ All b) ☐ Some* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

- 14) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

- 15) ☐ Notice of References Cited (PTO-892)
- 16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
- 18) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 19) ☐ Notice of Informal Patent Application (PTO-152)
- 20) ☐ Other:

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DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 7/19/01 has been entered.
2. Claims 1-8, 10-15, 37-39 are currently pending in this application.
3. The amendment G, filed on 7/19/01 has been fully considered and entered into the application.
4. Claims 1 and 10 have been amended by the amendment G, filed on 7/19/01.
5. The rejection of claims 1-8, 10-15, 37-39 under 35 U.S.C. 112, first paragraph have been withdrawn in view of amendments to the claims.
6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person

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having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

8. Claims 1-8, 10-15 and 37-39 are rejected under 35 U.S.C. 102(e) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Lam et al (US Patent 5,640,489).

Lam *et al* teach the synthesis of random bio-oligomers (which reads on diverse polymers, see abstract) which may be peptides or oligonucleotides or a peptide oligonucleotide chimera (*see col. 5, lines 8-17*) (refers to newly added limitation of the instant claims). Lam *et al* teach the synthesis of the oligomers using the split and combine method whereby individual beads are used to synthesize one polymer per bead (*i.e., see figure 1*). Lam *et al* teach synthesizing arrays of polymers using different protocols in order to compare the results of the synthetic process on the array produced. Lam *et al* also teach separately cleaving the collections of polymers from the support beads to form separate mixtures and measuring the components present via a property (UV absorbance in this instance) which reads on measuring a "property" (the composition) of the mixture of unbound polymers as an indicator of the efficiency of the synthesizing step (*see figure*

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3 and col. 34, line 60 - col. 35, line 55). In that the array of polymers produced in one method is compared to the array produced in the second method one array reads on a reference array. Lam *et al* also teach several alternative embodiments for the preparation of polymeric arrays. In that the 215 nm absorbance by the exemplified peptides in Figure 3 is due to the amide bonds of the backbone the polymers comprise a label as required by claim 39. [That the absorbance at 215 nm is due to the amide backbone is well known in the art. However, the examiner has attached pages 161-162 of *Spectrophotometric identification of Organic Compounds (2nd ed, 1967)* for applicants convenience which clearly evidences this assertion.]. Additionally, it is noted that the indole ring of tryptophan or the phenyl ring of phenylalanine can serve as a detectable label at 280 nm (*see Lam et al col. 33, lines 55-57*). Therefore, Lam *et al* additionally reads on instant claim 39. In that each of the peptides in the exemplified arrays contain a tryptophan they comprise a single isomer as required by claim 2. Lam *et al* also teach that it is known to prepare libraries where the length of the polymer (number of monomeric units) is different as required by claims 3-5, *see col. 38 lines 60-65*.

Lam *et al* teach the use of reverse phase HPLC to monitor the composition of the oligomer mixtures cleaved from the array, Lam *et al* render obvious the use of other well-known HPLC methods, which in view of applicants' disclosure of prior art teachings are notoriously well known and established in the art (*see pages 38 and 39 of the specification*). In addition, the analyses of mixtures of materials by gel electrophoresis as required in claim 5, especially the analysis of peptides and nucleotides is notoriously well known in the art as clearly evidenced by

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applicants' reliance on standard texts, laboratory manuals and manufacturers' literature, see page 38 and 39 of the specification.

Lam *et al* specifically recites the oligomers of the array can be oligonucleotides as required in claims 8 and 11 (*i.e.*, see col. 5, lines 8-17). Lam *et al* teach that the use of cleavable linkers, as required by claim 13, are well known in the art (*see col. 16, lines 10-40*). In that the peptides exemplified by Lam *et al* were detected by their absorbance at 215 nm (*see figure 3 left axis*) they clearly are comprised of a detectable label as defined by applicant on page 12 of the specification and required in claim 14. In that the backbone amide chromophore comprises a single isomer and alternatively the indole of tryptophan comprises a single isomer (which is also fluorescent) Lam *et al* reads on claims 14, 15 and 37-38. Lam *et al* also teach different embodiments polymer array libraries are known in the art including planar arrays (*i.e.*, *spatially addressable arrays of Fodor et al*), *see for example col. 3, lines 47-52*. Therefore, while the preparation of libraries on planar arrays and their analysis is not the preferred embodiment set forth in Lam *et al* it is an immediately envisioned embodiment and hence the reference anticipates the invention of the instant claims.

In the alternative, one could argue that Lam *et al* did not analyze the arrays of polymeric molecules on a substrate and hence conduct the methods set forth in the instant claims.

However, it would have been *prima facie* obvious to one of ordinary skill in the art at the time that the invention was made to analyze arrays made on planar supports by cleaving array members off and analyzing for their presence as taught by Lam *et al* because Lam *et al* teach the

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analysis of arrays of molecules which have been prepared and that planar arrays are known in the art. One of ordinary skill in the art would have been motivated to do so in order to be able to analyze the arrays made in different protocols which Lam *et al* teach is desirable. One of ordinary skill in the art would have reasonably expected to be successful as Lam *et al* had taught the analysis of molecules released from an array.

9. Claims 1-8, 10-15 and 37-39 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lam *et al* [5,640,489; 102(e) date of at least 7/2/91] in view of Holmes [US 5,679,773] and applicants' disclosure of the prior art teachings.

See the teachings of Lam *et al* and applicants' disclosure of the prior art teaching as applied to claims 1-8, 10-15 and 37-39 under 35 U.S.C 103(a) as being unpatentable over Lam *et al* in view of Fodor and applicants disclosure of the teachings of the prior art, *supra*.

Holmes *et al* teach the synthesis of polymer arrays on a substrates where each member of the polymer array occupies a different region of the substrate and the desirability of determining the fidelity of synthesis of such arrays (column 19, lines 33-58).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to monitor the synthesis of polymer arrays synthesized on a support as taught by Holmes using a method of analysis as taught by Lam *et al*, because Lam *et al* teach the desirability of monitoring polymer array synthesis in order to compare the methods utilized in the synthetic process (see example 7 "*Comparison of the claimed method with the conventional*

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method of peptide synthesis” starting in column 7 at line 60) which analyze mixtures of polymers cleaved from the support and Holmes teaches the desirability of determining the fidelity of array synthesis on planar supports by cleaving the polymers from the support. One of ordinary skill in the art would have been motivated to do so in order to compare array synthesis protocols and the resulting fidelity of array synthesis as suggested by Lam *et al* and Holmes. One ordinary skill in the art would reasonably have expected to be successful because the basic method of preparing an array of oligomers on supports, cleaving them to form a mixture of oligomers and analyzing them had already been conducted by Lam *et al*. One of ordinary skill in the art would also have reasonably expected the use of gel electrophoresis, and HPLC chromatography to be successful because these are notoriously well known methods of analysis which have been applied to oligomeric compounds such as peptides and nucleotides.

10. *Applicants’ arguments regarding the rejection of claims over Lam et al, filed 7/19/01 have been fully considered but they are not persuasive.*

Applicants’ assert that Lam et al does not teach or suggest a preselected array of diverse biological polymers, hereby the diverse polymers occupy different regions of the substrate. Lam is directed to a single bead acting as a single substrate having only a single biopolymer.

Applicants assert that Lam provides no guidance for creating diverse polymers on a substrate

Applicants assert that Lam et al do not teach or suggest to measure the presence of diverse unbound biological polymers as indicator of the efficiency of the synthesizing step.

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Applicants' arguments have been considered but are not found persuasive. The assertion that Lam et al provide no motivation to be modified to use a single bead arranged in a spatially defined pattern is not found persuasive because Lam et al clearly set forth the desirability of comparing synthesis protocols (i.e., determining the synthesis efficiency etc...) Applicants' assertion that Lam et al provide no guidance for creating diverse polymers on a substrate is not persuasive because Lam et al teach the method can be used for synthesis of random library as well as for the synthesis of peptide library that comprise a predetermined sequence (refers to preselected array of the instant claims) (see column 10, lines 57-59). Applicants arguments that Lam et al teach only random library is based on column 39, column 43, column 46, whereas Lam et al teach the synthesis of predetermined peptides in column 10, and example 11, example 14. Therefore, the rejection is maintained.

11. *Applicants' arguments filed 7/19/01, regarding the rejection of claims over Lam et al and Holmes et al, have been fully considered but they are not persuasive.*

Applicants assert that Lam provides no guidance for creating diverse polymers on a substrate. Applicants assert that Lam et al teaches against the use of preselected array of diverse biological polymers on a solid support. Applicants argue that Lam et al teachings require addition of a set of amino acids to aliquots of reagents to produce a peptide, wherein each bead contains a single biopolymer. Applicants conclude that Holmes fail to cure the deficiencies of Lam et al

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Applicants assertions have been considered but are not persuasive, because Lam et al in column 7, line 14 teach the a ‘biooligomer library may be composed of a predetermined limited number of subunits; and in column 10, lines 57-59 teach that “this method may be used for synthesis of random peptide libraries as well as for the synthesis of a peptide library that comprised of predetermined sequences.”. Applicants assertion that Lam et al require a set of amino acids to produce a library is not persuasive. Lam et al in column 10, lines 57-59, do not teach that a set of amino acids are required as asserted by applicants. Lam et al in column 10, in lines 59 and further, teach that “the synthesis of predetermined sequences involve the use of specific N-Boc-, N-Fmoc, or other appropriately protected amino acids during specific coupling steps”, which would be interpreted as the use of specific (determined by the selected sequence) protected amino acids, not the use of random amino acids and would not result in random library as applicants interpretation.

The assertion that Lam et al are limited to a single biopolymer to a bead, the argument fails to consider the teachings of Holmes. Applicants assertion Lam et al provide no guidance for creating diverse polymers on a substrate is not persuasive as it does not take into account the teachings of Holmes which were cited for this purpose. Therefore, the rejection is maintained for the reasons above and for the reasons of record.

12. No claims are allowed.

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13. The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to P. Ponnaluri whose telephone number is (703) 305-3884. The examiner can normally be reached on Monday to Thursday from 6.30 AM to 4.00 PM. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jyothsna Venakt, Ph.D., can be reached on (703) 308-2439. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

P. Ponnaluri
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28 September 2001


PADMASHRI PONNALURI
PRIMARY EXAMINER